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In Vitro Susceptibilities of *Aeromonas hydrophila*, *Aeromonas sobria*, and *Aeromonas caviae* to 22 Antimicrobial Agents

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MICs of 22 antimicrobial agents for 60 strains of three *Aeromonas* species were determined by a microdilution method. The newer cephalosporins such as moxalactam, cefotaxime, and cefoperazone, the aminoglycosides, and chloramphenicol, tetracycline, nitrofurantoin, and trimethoprim-sulfamethoxazole inhibited most of the strains studied. Within the genus, *A. hydrophila* was more resistant than either *A. caviae* or *A. sobria* to the antibiotics tested.

Aeromonas hydrophila, a ubiquitous waterborne organism, has been implicated in a variety of clinical infections including gastroenteritis, cellulitis, and bacteremia in immunocompromised or cirrhotic individuals (4). Although the genus is well-defined, the exact number of distinct species making up the motile *Aeromonas* group (often referred to as the *A. hydrophila* complex) remains unknown. Recent numerical taxonomy and DNA-DNA reassociation studies suggest that at least three species of *Aeromonas*, namely, *A. hydrophila*, *A. sobria*, and *A. caviae*, should be recognized (13, 14). The relevance of this proposal is supported by further clinical and microbiologic studies showing that all three species can be recovered from human infections (8). In addition, several studies suggest that the majority of *A. hydrophila* and *A. sobria* strains recovered from gastroenteritis are enterotoxigenic (1, 2, 15). Invasive potential among the three aeromonal species as judged by their frequency of recovery from blood, their 50% lethal dose for mice and fish, and their exoenzymatic activity also appears to differ substantially (3, 5, 9).

Previous antimicrobial susceptibility studies of *Aeromonas* were performed with isolates collectively designated *A. hydrophila* (6, 7, 12). Since newer taxonomic criteria have enabled the correlation of different *Aeromonas* species with distinct infectious processes and virulence potential, the species-associated antibiotic susceptibility patterns may serve as important therapeutic and diagnostic guidelines. In this regard we studied the antimicrobial susceptibility of the three *Aeromonas* species.

Sixty *Aeromonas* strains of human origin were tested in this study, and their respective sources of isolation are listed in Table 1. Of these strains, 39 were recovered in the New York City area, 14 were obtained from the gastrointestinal contents of children in Thailand and were kindly provided by P. Echeverria, and 7 from various clinical sources were submitted by T. Overman. Clinical information was available on 19 of the New York City isolates. Three patients (two with *Aeromonas* bacteremia and one with *Aeromonas* gastroenteritis) were receiving antimicrobial therapy either simultaneously or just before the isolation of their respective strains. All isolates were recovered in mixed culture with the exception of two bacteremic strains and one isolate recovered in pure culture from a patient with *Aeromonas* wound infection. The clinical significance of these 19 isolates was determined by previously defined criteria (8), and the results were as follows: primary or secondary pathogen (n = 15, 79%), colonization (n = 1, 5%), and undetermined significance (n = 3, 16%). Species of the isolates were determined by a modification of the original criteria of Popoff and Véron as previously described (9). MICs were determined by a microdilution method in modified Eugon (cation supplementation for aminoglycosides and thymidine phosphorylase supplementation for trimethoprim-sulfamethoxazole) broth (Uniscept MIC Plus; Analytab Products, Plainview, N.Y.) with an inoculum of approximately 10^6 CFU/ml.

Results of testing 20 isolates of each species against each of 22 antimicrobial agents are listed in Table 2. Breakpoints for susceptible, intermediate, and resistant categories were determined by tentative NCCLS standards with the susceptible category used in discussing percent susceptible (11). All *Aeromonas* spp. studied were susceptible to gentamicin, amikacin, chloramphenicol, trimethoprim-sulfamethoxazole, tetracycline, and nitrofurantoin and uniformly resistant to methicillin, erythromycin, clindamycin and vancomycin. For 7 of 60 *Aeromonas* isolates, the MIC of tobramycin was >8 μg/ml. With beta-lactam antibiotics, all three species were resistant to penicillin, ampicillin, and carbenicillin: 50% of all strains tested, however, were susceptible to piperacillin and mezlocillin. The third-generation cephalosporins moxalactam, cefotaxime, and cefoperazone were uniformly active against the 60 isolates, with MICs ranging from 2 to 64 μg/ml. Second-generation cephalosporins (cefoxitin and cefamandole) inhibited approximately 50% of the 60 strains tested.

Of the three species tested, *A. hydrophila* was more resistant to the penicillins and cephalosporins than either *A.*

TABLE 1. Sources of *Aeromonas* isolates used in this study

Source of isolation	No. of isolates		
	A. hydrophila	*A. caviae*	*A. sobria*
Stool	8	12	11
Blood	1	2	8
Wound	9	5	1
Respiratory tract	2	1	0

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TABLE 2. In vitro susceptibility of 60 *Aeromonas* isolates to 22 antimicrobial agents

Antimicrobial agent	*A. hydrophila* (*n* = 20)			*A. caviae* (*n* = 20)			*A. sobria* (*n* = 20)		
	Range[a]	MIC_{50}[a]	MIC_{90}[a]	Range	MIC_{50}	MIC_{90}	Range	MIC_{50}	MIC_{90}
Amikacin	≤2–4	≤2	≤2	≤2–4	≤2	≤2	≤2–8	≤2	≤2
Ampicillin	≥16	≥16	≥16	2–≥16	≥16	≥16	2–≥16	≥16	≥16
Carbenicillin	32–≥512	128	≥512	≤8–≥512	32	256	≤8–≥512	256	≥512
Cefamandole	2–≥32	2	≥32	≤2–≥32	≤2	16	≤2–8	≤2	≤2
Cefoperazone	≤4–8	≤4	≤4	≤4–64	≤4	≤4	≤4	≤4	≤4
Cefotaxime	≤2	≤2	≤2	≤2	≤2	≤2	≤2	≤2	≤2
Cefoxitin	≤2–≥32	≤2	≥32	≤2–≥32	≤2	8	≤2–16	≤2	≤2
Cephalothin	≤2–≥32	≥32	≥32	8–≥32	≥32	≥32	≤2–≥32	≤2	≥32
Chloramphenicol	≤1–8	≤1	≤1	≤1	≤1	≤1	≤1	≤1	≤1
Clindamycin	≥8	≥8	≥8	≥8	≥8	≥8	≥8	≥8	≥8
Erythromycin	≥8	≥8	≥8	2–≥8	≥8	≥8	2–≥8	≥8	≥8
Gentamicin	≤0.5–4	≤0.5	1	≤0.5–2	≤0.5	1	≤0.5–>8	≤0.5	1
Methicillin	≥16	≥16	≥16	≥16	≥16	≥16	4–≥16	≥16	≥16
Mezlocillin	≤16–256	≤16	256	≤16–128	≤16	≤16	≤16–256	≤16	256
Moxalactam	≤4	≤4	≤4	≤4–8	≤4	≤4	≤4	≤4	≤4
Nitrofurantoin	≤16	≤16	≤16	≤16	≤16	≤16	≤16	≤16	≤16
Penicillin	≥16	≥16	≥16	4–≥16	≥16	≥16	4–≥16	≥16	≥16
Piperacillin	≤8–256	≤8	256	≤8–512	≤8	16	≤8–256	≤8	64
Tetracycline	≤1–2	≤1	≤1	≤1–2	≤1	≤1	≤1	≤1	≤1
Tobramycin	≤0.5–≥8	2	≥8	≤0.5–8	≤0.5	1	≤0.5–≥8	≤0.5	4
Trimethoprim-sulfamethoxazole	≤1/19–2/38	≤1/19	≤1/19	≤1/19–4/76	≤1/19	≤1/19	≤1/19	≤1/19	≤1/19
Vancomycin	≥8	≥8	≥8	≥8	≥8	≥8	≥8	≥8	≥8

[a] Micrograms per milliliter.

caviae or *A. sobria*. Ninety percent of *A. caviae* and *A. sobria* strains were inhibited at levels of 16 and 64 μg of piperacillin per ml, respectively, while 256 μg of piperacillin per ml was required to inhibit 90% of the *A. hydrophila* strains (MIC_{90}). Similarly, a higher concentration of cefamandole (>32 μg/ml) was required to inhibit 90% of the *A. hydrophila* isolates as compared with *A. caviae* (16 μg/ml) or *A. sobria* (<2 μg/ml). Greater than 32 μg of cefoxitin per ml was required to inhibit 90% of the *A. hydrophila* isolates as compared with *A. caviae* (8 μg/ml) or *A. sobria* (<2 μg/ml). A unimodal distribution of strains was reflected in the higher MIC_{90}s of these antibiotics for *A. hydrophila*.

The most striking difference among the species was seen in susceptibility to cephalothin. There were 4 of 20 *A. hydrophila* strains and only 1 of 20 *A. caviae* isolates that were susceptible to 8 μg of cephalothin per ml. In contrast, for 13 of 20 *A. sobria* strains the MIC was <2 μg/ml, and for one additional strain the MIC of this antibiotic was 4 μg/ml ($P < 0.005$). Although this observation requires further investigation, cephalothin susceptibility may prove to be a useful marker for *A. sobria*.

Recently, McNicol and colleagues (10) reported that 57% of the environmental *Aeromonas* isolates recovered in Bangladesh were resistant to multiple antibiotics including tetracycline and that the resistance appeared to be plasmid mediated. In addition, high-level resistance to chloramphenicol was also noted. Similar resistance patterns have been observed in *Aeromonas* isolates recovered from the Chesapeake Bay. In our study, no antibiograms similar to those described above were noted because all clinical isolates were susceptible to both drugs. These differences may be related to the source or species of *Aeromonas* recovered, the method of isolation, the frequency of use of certain antimicrobial agents in a specific geographic area, or to other unknown factors.

Comparative antibiograms of taxonomically defined

Aeromonas species reveal that most isolates are susceptible to a wide range of antibiotics, excluding beta-lactam agents and those normally active against gram-positive bacteria. As judged by MIC, higher levels of resistance to various antibiotics were observed especially among *A. hydrophila* strains when compared with either *A. sobria* or *A. caviae*. Taken together, these data suggest that identification of *Aeromonas* isolates to the species level may have important implications in the selection of definitive species-oriented therapy.

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